neutropenia or engraftment not occurring by day +21. Accrual target was 20 patients for each group with a planned interim analysis after ~10 patients. For each pilot patient, a control was randomly selected from 2013; controls were matched by age, graft source, diagnosis and cell dose. Implementation of the pilot was the effort of a multi-disciplinary team including physicians, mid-level providers, nurses, clinical pharmacists, data and quality assurance personnel.

Findings: For the auto and allo MAC groups, interim analysis revealed that omission of G-CSF led to longer LOS and longer time to neutrophil engraftment (see Table). The interim analysis of the allo RIC group appears to be comparable for the length of stay and neutrophil engraftment.

Discussion: Any cost savings of not using G-CSF are likely to be offset by the longer duration of post-transplant hospitalization and possible increased risks due to longer periods of neutropenia. Based on our findings, the pilot has been discontinued for auto and allo MAC transplants, where we will continue to use G-CSF starting on Day +5 to promote engraftment. This pilot will accrue the planned 20 patients for allogeneic RIC patients before a final analysis is performed.

PHARMACY

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Folinic Acid Rescue after Methotrexate Graft Versus Host Disease Prophylaxis to Reduce Mucositis and Improve the Probability of Day +11 Methotrexate Administration - Role of the Hematopoietic Cell Transplant Pharmacist in Development of Program Guidelines

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Background: Methotrexate (MTX) is routinely utilized for prophylaxis of graft versus host disease (GVHD). MTX may contribute to mucositis and delayed engraftment. Severe mucositis results in MTX dose reduction, holding day +6 and/or day + 11, addition of folinic acid (FA), or the use of dexamethasone. Delivery of day +11 MTX has been reported to be important in reducing the risk of aGVHD. FA administration after MTX doses has been shown to reduce MTX toxicity. In an effort to reduce the incidence of mucositis to improve the likelihood of administering day +11 MTX and to provide a consistent treatment guideline, the Hematopoietic Cell Transplant (HCT) program director enlisted the help of the HCT pharmacist to review the data and recommend guidelines.

Methods: A review of the literature for post-MTX FA use was performed and presented at an HCT program education session. FA dosing, time of initiation post MTX, schedule and number of doses were discussed. The HCT providers agreed to follow the HCT pharmacist recommendation of FA 10mg/m^2 IV every 6 hours x 3 doses starting 12 hours after each MTX dose (day +1, +3, +6 and +11) with myeloablative (MA) conditioning regimens. All patients received tacrolimus. Data was retrospectively collected in 2013 after the FA guideline was adopted and compared to consecutive patients receiving MA regimens from a control group in 2012. The primary endpoint was administration of full dose day +11 MTX. Secondary endpoints were rates of aGVHD, cGVHD, total parenteral nutrition (TPN) use, patient controlled analgesia (PCA) use, transplant-related mortality (TRM), relapse and overall survival (OS).

Results: The FA group consisted of 27 patients while there were 31 in the control. Patients in the FA group were more likely to receive full dose day +11 MTX as compared to control, 85.2% vs 48.4% (p=0.0025) and were less likely to require PCA, 63% vs. 87.1% (p=0.03). There was no significant difference in rates of TPN use (48.2% vs. 58.1%), grade II-IV aGVHD at day 100 (50.4% vs. 30.5%), cGVHD (19.9% vs. 27.7%), cumulative incidence of relapse (10.8% vs. 8.6%), TRM at 1 year (13.1% vs. 19.5%) and OS at 1 year (77.9% vs. 75.9%) for the FA group and control, with a median follow-up of 465 days and 670 days, respectively.

Discussion: Patients experienced less mucositis and were more likely to receive full dose day + 11 MTX after implementation of the FA guideline. This was also supported by a statistically significant decrease in PCA use. Other endpoints trended in a favorable direction, but did not reach statistical significance. The development and utilization of the program guideline improved consistency of care, improved staff satisfaction and decreased patient discomfort. HCT pharmacists play an important role in the review of literature and development of program guidelines.

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Evaluation of the Impact of Anti-Thymocyte Globulin (ATG) on Post-Hematopoietic Cell Transplant (HCT) Outcomes in Patients Undergoing Allogeneic HCT

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Background: Anti-thymocyte globulin (ATG) is often incorporated into allogeneic stem cell transplant (alloHCT) conditioning regimens to prevent graft-versus-host disease (GVHD). Literature regarding the effect of ATG on outcomes is mixed; some data suggests an improvement in GVHD control with ATG use, but other data shows a reduction in overall survival, particularly in the reduced intensity setting. This study evaluates the impact of ATG on infection, GVHD, relapse, and mortality rates in adult alloHCT patients.

Methods: A retrospective review of 250 adult alloHCT patients at our institution (125 unrelated/mismatched donor recipients received ATG, 125 matched related donors did not) between 2006 and 2013 was performed. Charts were reviewed for ATG use, demographics, infections (bacterial, viral, fungal), infection source, GVHD, day-180 relapse, and day-180 mortality. The primary endpoint was infection rate; secondary endpoints included mortality and GVHD.

Results: Factors with significant impact on infection incidence were conditioning type (Myeloablative (MAC) > Reduced Intensity (RIC), p=0.0105), age (p=0.0245), and use of ATG (p=0.0185). MAC was associated with greater

incidence of infection (median 3 infections vs. RIC median 2 infections, p=0.0001). Infection incidence was significantly increased in patients receiving ATG compared to those not receiving ATG (median 3 vs. 2, p=0.0003). The relative increase in infections with ATG was more pronounced in RIC (+ATG median 3 vs −ATG median 1) than in MAC (+ATG median 4 vs. −ATG median 3). In both RIC and MAC, ATG use was associated with increased numbers of CMV (112 vs. 61), HHV6 (47 vs. 13), and HSV (32 vs. 8) infections. The relative increase in infection incidence for +ATG patients in RIC (CMV 2.5-fold, HHV6 10.5-fold, HSV 6.5-fold increase) was greater than the increase seen for +ATG patients in MAC (CMV 1.46-fold, HHV6 2.36-fold, HSV 3.17-fold increase).

Similar rates of severe (grade 3-4) aGVHD were observed in +ATG patients compared to −ATG patients (17.5% vs. 14.95%, p=0.72) through day 180, indicating a potential protective effect of ATG in unrelated/mismatched transplants. In RIC, a nonsignificantly greater proportion of +ATG patients developed severe aGVHD (19.4%) compared to −ATG patients (12.9%).

The rates of relapse/death were not different between ATG groups (29.91% for −ATG and 39.68% for +ATG), and groups had similar mean times to relapse (148 days for −ATG and 138 days for +ATG). At 180 days, survival was 83.2% for −ATG and 71.4% for +ATG (p=0.0426).

Conclusion: Our study demonstrates that ATG use increases infection rates in alloHCT patients, with greater impact in the RIC setting. Although relapse rates were similar between groups, the 180-day mortality for +ATG was significantly greater than −ATG, suggesting that infectious complications may impact mortality associated with ATG.

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Comparison of Outcomes of Two Preparative Regimens for Lymphoma Patients Who Are Receiving Autologous Hematopoietic Stem Cell Transplantations

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Background: Current literature supports the use of hematopoietic stem cell transplants (hSCT) over salvage chemotherapy for patients with lymphoma who have recurrent disease or are at high risk of relapse. Few studies have been published directly comparing preparative regimens, thus most institutions select regimens based on associated toxicities. At our institution, Busulfan/Cyclophosphamide (Bu-Cy) was historically used as the preparative regimen for patients with lymphoma. A transition was made in 2009 to favor the theoretically less toxic Carmustine/Etoposide/Cyclophosphamide (CBV) regimen for older patients.

Objective: Compare the tolerability and efficacy of Bu-Cy and CBV as they pertain to autologous stem cell transplants in older patients.

Methods: We report a retrospective review of institutional data evaluating the safety and efficacy of Bu-Cy and CBV in patients with lymphoma receiving an autologous hSCT between January 2005 and January 2014. Patients were excluded if they were less than 60 years of age. The primary outcome was the incidence of grade 3 and 4 toxicities per the CTCAE v4.03. Secondary outcomes included progression-free and overall survival.

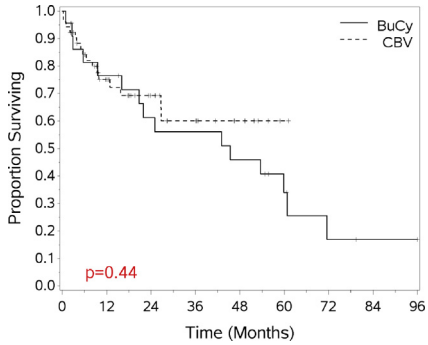

Figure 1. Time to mortality

Results: Seventy-five patients were available for analysis, 23 received Bu-Cy and 52 received CBV. Patients who received Bu-Cy experienced an average of 1.6 severe or life-threatening toxicities per patient compared with 1.7 for those who received CBV. There was no difference in progression-free (BuCy 86% vs CBV 95%) or overall survival (BuCy 96% vs CBV 94%) at 60 days; however, there was a trend toward increased progression-free survival (BuCy31% vs CBV 68%) at three years Figure 1) and this trend was supported by the increased time to relapse (BuCy 22.7 vs CBV 61.2 months) (Figure 2).

Conclusions: This review demonstrates no difference in terms of tolerability or efficacy between Bu-Cy and CBV; however, there is a trend towards improved relapse free survival with CBV. Future studies are needed to compare other utilized preparative regimens.

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Dose-Escalated G-CSF Dose Not Improve Resolution of Neutropenia Compared to Standard-Dose G-CSF Following Autologous Stem Cell Transplantation

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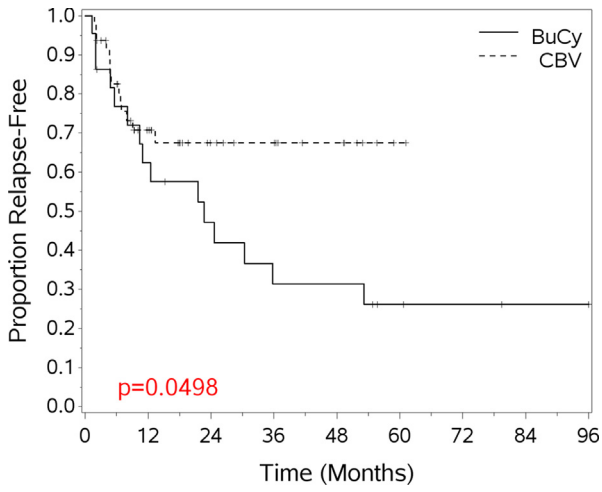

Figure 2. Time to relapse